Comparative Study of Methotrexate Topical Gel and Calcipotriol Topical Gel for Treatment of Psoriasis

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Abstract- Psoriasis is a chronic inflammatory skin condition characterized by red, scaly, and itchy plaques. Topical therapy is preferred for mild to moderate cases. Methotrexate acts as an antimetabolite, reducing inflammation, while Calcipotriol is a vitamin D analogue controlling abnormal keratinocyte growth. This review compares both gels in terms of efficacy, safety, and practical use. Comparative studies have reported that Calcipotriol shows faster onset of action within 2 weeks, whereas Methotrexate provides longer remission periods. Combination therapies showed superior PASI reduction and lower recurrence rates. [1]

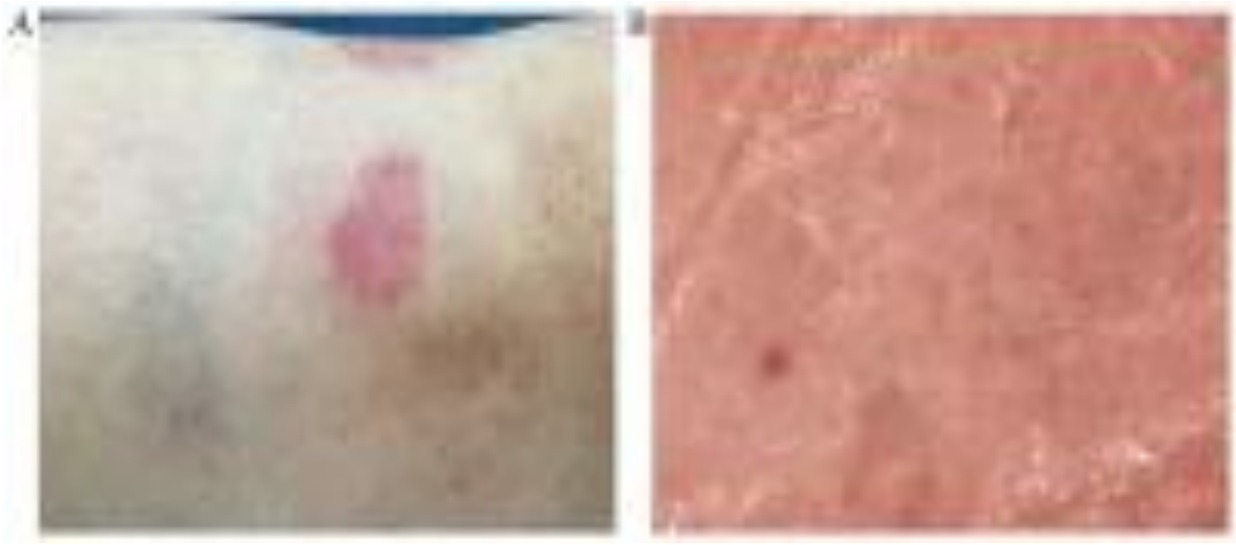
Keywords- calcipotriol; methotrexate Pasi score; psoriasis; vitamin d.

I. INTRODUCTION

Psoriasis affects roughly 2–3% of people worldwide and is caused by immune system dysfunction that accelerates skin cell growth. It often results in discomfort, visible lesions, and reduced quality of life. Topical treatments are the preferred first-line therapy, especially for mild to moderate cases, before systemic medications or biologics are considered. Methotrexate (MTX) and Calcipotriol (CPL) topical gels have been widely studied and show promising results in reducing plaques and improving skin condition. According to WHO reports, psoriasis affects approximately 125 million people worldwide, with increasing prevalence due to stress, genetics, and immune factors.
[2-4][2 3,4]

II. PATHOPHYSIOLOGY

In psoriasis, T-cells become overactive, releasing cytokines such as TNF-α, IL-17, and IL-23. This triggers excessive keratinocyte proliferation, leading to thickened plaques and scaling. Normally, the epidermis renews every 28 days, but in psoriasis, this cycle shortens to 4–5 days, resulting in rapid plaque formation and inflammation.[5] Elevated cytokines like TNF-α, IL-17, and IL-23 promote keratinocyte hyperproliferation. The Th1 and Th17 immune pathways are considered central to psoriasis pathogenesis. *[6-7]*[6,7]

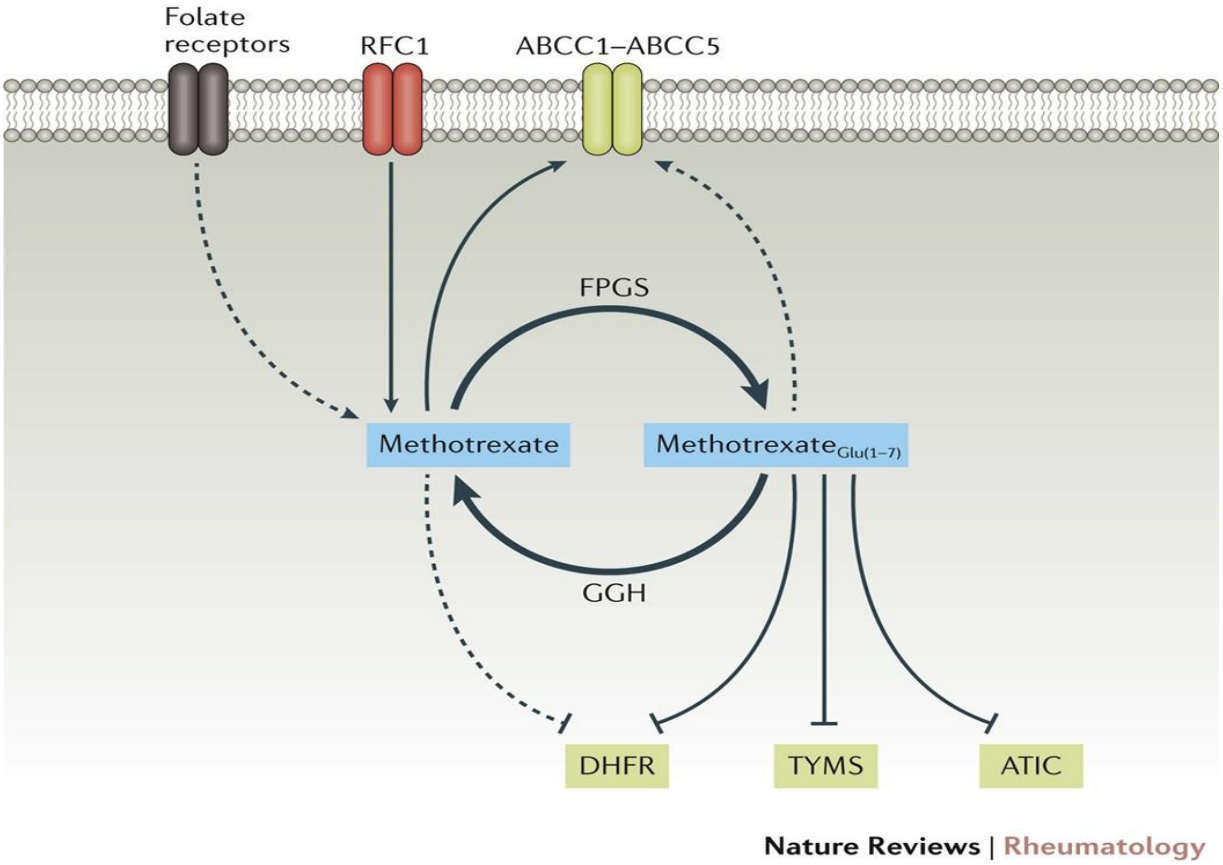


p *Figure 1. Plaque psoriasis*

III. METHOTREXATE TOPICAL GEL

Methotrexate inhibits dihydrofolate reductase, stopping DNA synthesis and reducing keratinocyte proliferation. Topical MTX limits systemic absorption, reducing the risk of liver or blood-related side effects seen with oral methotrexate. Studies have demonstrated that 1% MTX gel significantly decreases plaque thickness and redness. Recent studies have developed methotrexate nanogels and liposomal systems that enhance penetration and minimize irritation, showing PASI score improvement up to 70% in 8 weeks[8]

Mechanism of action of methotrexate



Moa of Methotrexate

Advantages

- Localized action reduces systemic toxicity
- Effective for inflammatory plaques
- Well-tolerated with minimal side effects[1]

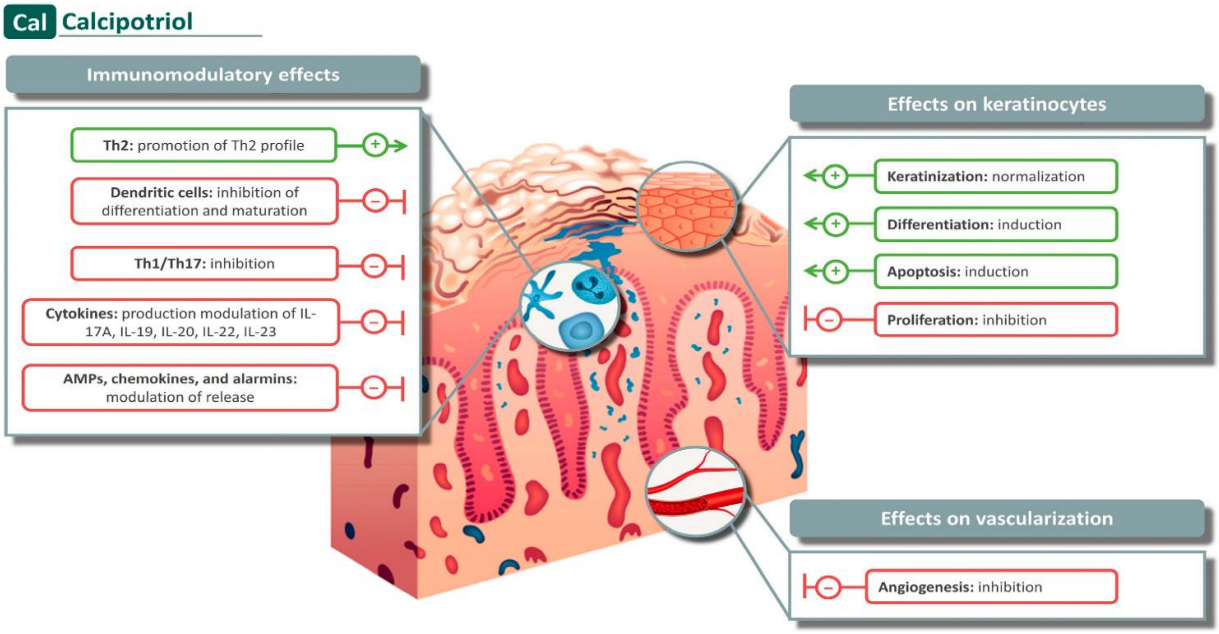
Disadvantages

- Slow absorption through thick skin
- May need enhancers or nanocarriers for better penetration *[9-10]*[9,10]

IV. CALCIPOTRIOL

Calcipotriol binds to vitamin D receptors in skin cells, regulating keratinocyte growth and differentiation. It is particularly effective in mild to moderate psoriasis, decreasing scaling and plaque thickness. Clinical studies show significant improvement in Psoriasis Area and Severity Index (PASI) within 6–8 weeks Calcipotriol combined with methotrexate or corticosteroids provides synergistic effects by reducing inflammation and scaling more effectively than monotherapy.[11-12][11,12]

Mechanism of Action of Calcipotriol



Moa of calcipotriol [13]

Advantages

- Faster relief of scaling and redness
- Safe for long-term use
- Improves overall skin appearance

Disadvantages

- May cause mild burning or irritation
- Less effective in severe cases[14]

Comparative Table

Parameter	Methotrexate Gel	Calcipotriol Gel
Mechanism	Inhibits DNA synthesis	Vitamin D analogue
Onset	2–4 weeks	1–2 weeks
Efficacy	Moderate-high	High
Side Effects	Mild itching/dryness	Mild irritation/burning
Compliance	Moderate	High

[13][15]

Evaluation Parameter Charts

Parameter	Methotrexate Gel	Calcipotriol Gel
PASI Reduction	60–70% in 8 weeks [2]	65–75% in 6–8 weeks
Erythema	Gradual reduction	Faster reduction][16]
Scaling	Noticeable after 4 weeks	Faster, 2–3 weeks
Skin Thickness	Epidermis thinning[17][17]	Normalized epidermis
Onset	2–4 weeks[18][18]	1–2 weeks
Duration	Long-lasting[19][19]	Relapse 4–6 weeks[14][14]
Satisfaction	Moderate[20][20]	High[21][21]
Safety	Mild itching/dryness[2,][2]	Mild irritation[2,22][2,22]
Systemic Absorption	<2%	Negligible
Combination	Effective with CPL[3][3]	Effective with MTX[3,23][3,23]

V. COMBINATION THERAPY

Using Methotrexate and Calcipotriol together improves plaque clearance. Methotrexate targets inflammation; Calcipotriol regulates keratinocyte proliferation. Nanocarrier formulations enhance absorption and minimize irritation. Current research focuses on hybrid MTX–CPL nanocarrier systems that improve percutaneous absorption and provide sustained release, reducing relapse frequency.*[24]*[24]

VI. SAFETY PROFILE

Both gels are safe. Methotrexate has minimal systemic absorption; Calcipotriol is well-tolerated, though excessive use may rarely cause hypercalcemia. Patient

adherence remains a challenge due to daily application requirements. Future approaches like microneedle-assisted gels and transdermal patches may enhance delivery efficiency and compliance.*[25]*[25]

VII. DISCUSSION

Methotrexate works slower but is effective for chronic inflammatory plaques, while Calcipotriol provides faster symptomatic relief. Combination or nanogel therapy can improve outcomes, reduce relapse, and enhance patient satisfaction.*[26]*[26]

VIII. CONCLUSION

Methotrexate and Calcipotriol gels are effective and safe for mild to moderate psoriasis. Methotrexate suits chronic plaques, Calcipotriol is better for rapid scaling reduction. Combination therapy or nanogel formulations may further improve outcomes. Further clinical studies are needed to validate long-term efficacy and safety of novel Methotrexate–Calcipotriol nanocarrier combinations.[*27-30]* [27–30]

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